

**REMARKS**

Reconsideration of this application is respectfully requested.

**A. Status of Claims**

Claims 71, 76, and 77 are amended. Claims 71-77 are pending and stand rejected.

The claims have been amended to recite “wherein, the first and second recombination DNA sequences direct homologous recombination events between the first and second endogenous DNA sequences in the genome of the mammalian cell upon introduction of the DNA construct into the mammalian cell, such that the first and second insertion DNA sequences are inserted into the genome of the mammalian cell between the first and second endogenous DNA sequences.” That amendment finds support throughout the application as filed, such as at page 4, lines 1-13. The amendments do not introduce new matter.

**B. Claim Objection**

Claim 77 was objected to as lacking a period. Applicant thanks the Examiner for pointing out that oversight and has amended claim 77 to include a period.

**C. Rejection Under 35 U.S.C. § 112, Second Paragraph**

Claims 71-77 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Action at Item 3. Specifically, the Examiner is concerned that the recitations of (i) “recombination DNA sequences,” and (ii) “*the* first and second

endogenous sequences are *adjacent to* a desired insertion site in the genome of the mammalian cell” (emphasis added) do not define the metes and bounds of the claims. Applicant has amended claims 71, 76, and 77 to recite “wherein, the first and second recombination DNA sequences direct homologous recombination events between the first and second endogenous DNA sequences in the genome of the mammalian cell upon introduction of the DNA construct into the mammalian cell, such that the first and second insertion DNA sequences are inserted into the genome of the mammalian cell between the first and second endogenous DNA sequences.” Applicant submits that that language defines the metes and bounds of the recombination DNA sequences recited in the claims and also of the relationship between the “the first and second endogenous sequences” and the “insertion site in the genome of the mammalian cell.” Accordingly, that rejection may be withdrawn.

**D. Rejection Under 35 U.S.C. § 112, First Paragraph**

Claims 71-77 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly introducing new matter. Action at Item 4. Specifically, the Examiner is concerned that the term “recombination DNA sequences” introduces new matter.

Applicant has amended the claims to recite “wherein, the first and second recombination DNA sequences direct homologous recombination events between the first and second endogenous DNA sequences in the genome of the mammalian cell upon introduction of the DNA construct into the mammalian cell, such that the first and second insertion DNA sequences are inserted into the genome of the mammalian cell between the first and second endogenous DNA sequences.” Applicant submits that that

added language makes clear that "recombination DNA sequences" is used in the claims in a manner consistent with how such DNA sequences are described throughout the application. Applicant agrees with the Examiner that the term does not literally appear in the specification, but Applicant is using the term to define vector sequences that function to "direct homologous recombination events between the first and second endogenous DNA sequences in the genome of the mammalian cell upon introduction of the DNA construct into the mammalian cell, such that the first and second insertion DNA sequences are inserted into the genome of the mammalian cell between the first and second endogenous DNA sequences," as recited in the claims. Such sequences are fully disclosed in the application as filed and the claims do not include new matter. Accordingly, this rejection should be withdrawn.

**E. Rejections Under 35 U.S.C. § 103(a)**

Various groupings of claims 71-77 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Mansour et al., "Introduction of a lacZ reporter gene into the mouse int-2 locus by homologous recombination," *Proc Natl Acad Sci USA*. 87(19):7688-92, 1990 ("Mansour") in combination with various additional references. Action at Items 12-16. Applicants traverse those rejections.

Each of the rejections for alleged obviousness depends on the disclosure of Mansour. However, Mansour is not prior art to this application.

This application is a continuation of Application No. 10/639,754, filed August 13, 2003, which is a continuation of Application No. 08/466,699, filed June 6, 1995 (now Patent No. 6,638,768), which is a continuation of Application No. 08/301,037, filed

September 6, 1994, (now Patent No. 6,528,313), which is a continuation of Application No. 08/048,056, filed April 19, 1993, which is a continuation of Application No. 07/598,679, which was filed on March 19, 1990, as PCT/FR90/00185, and which claimed the benefit of priority to FR 89 03630, filed March 20, 1989. Therefore, the priority date of this application is March 20, 1989, and the United States filing date is March 19, 1990. Mansour was published after both of those dates, in October of 1990.

Because Mansour is not prior art to this application, the rejections for alleged obviousness should be withdrawn.

**F. Non-Statutory Double Patenting**

Claims 71-77 stand provisionally rejected for alleged non-statutory double patenting over claims 90, 99, and 108 of co-pending Application No. 10/639,754. Applicant acknowledges the rejection. Applicant is considering whether a Terminal Disclaimer is appropriate and will address this issue at such time as a conflicting claim is found otherwise allowable.

**G. Conclusion**

Applicant respectfully submits that claims 71-77 are in condition for allowance. Issuance of a Notice of Allowance is earnestly requested.

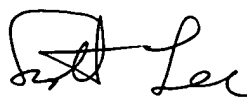
If there is any fee due in connection with the filing of this Reply, please charge the fee to our Deposit Account 06-0916.

Respectfully submitted,

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By: \_\_\_\_\_



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